

In the Claims:

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1. (amended) A method for treating a heterogeneous population of cancer cells in a living host by at least one of a first therapeutic agent and an additional therapeutic agent, the living host [being] including normal cells growing in a normal extra-cellular matrix having at least collagen and fibronectin, the heterogeneous population of cancer cells growing in a cancer-altered extra-cellular matrix having at least cancer-altered antigenic epitopes, the heterogeneous population of cancer cells endogenously making and converting products including at least sulphated glycosaminoglycans, natural intra-cell enzymes in the lysosomes, and having natural intra-cellular material including DNA, histone, and complexes of DNA-histone, the DNA, histone, and complexes of DNA-histone having antigenic epitopes, the heterogeneous population of cancer cells including at least four sub-populations of cancer cells:

the first sub-population of cancer cells being first target cancer cells each having a first antigenic receptor which is substantially specific to a cancer cell and which is capable of binding a first targeting agent, the first antigenic receptor being incapable of endocytosis when the first targeting agent binds to the first antigenic receptor;

a second sub-population of cancer cells being the second target cancer cells each having a second antigenic receptor which is substantially specific to a cancer cell and which is incapable of endocytosis;

a third sub-population of cancer cells being the third target cancer cells each having a high sensitivity to being killed by the natural system of the living host and [a high sensitivity to being killed by the natural system of the living host] an administered cell killing process;

a fourth sub-population of cancer cells being non-target cancer cells which are the remainder of the heterogeneous population of the cancer cells; and

the normal cells of the living host [in addition] endogenously making and containing products including at least sulphated glycosaminoglycans, [manual] natural intra-cellular enzymes in the lysosomes, and natural intra-cellular material including DNA, histone, and complexes of DNA-histone, the DNA, histone, and complexes of DNA-histone having antigenic epitopes, the normal cells including at least two sub-populations of normal cells:

the first sub-population of normal cells being the first target normal cells having the first antigenic receptor which is capable of binding the first targeting agent, the first antigenic receptor being incapable of endocytosis when the first targeting agent binds to the first antigenic receptor;

a second sub-population of normal cells being non-target normal cells which are the remainder of the normal cells;

the method comprising the steps of:

introducing into the living host a first bispecific reagent having two moieties, a first moiety which is a non-mammalian enzyme moiety being a first enzyme moiety, the first bispecific reagent further having a second moiety including a

targeting agent moiety which has a substantial affinity for the first antigenic receptor of the first target cancer cells and the first target normal cells;

permitting the first bispecific reagent to bind to the first antigenic receptor of the first target cancer cells and of the first target normal cells, the first bispecific reagent being received and bound at the first antigenic receptor of the first target cancer cells and of the first target normal cells, the first bispecific reagent thereby being retained in [the extra-cellular fluid] its bound location for an extended period of time which enables the first enzyme moiety to convert a substantial amount of the first therapeutic agent in the extra-cellular fluid into an insoluble non-digestible precipitate which is a first extra-cellular precipitate, the first extra-cellular precipitate being capable of remaining in the extra-cellular fluid adjacent to the first bispecific reagent for an extended period of time.;

administering to the living host the first therapeutic agent which is a soluble precipitable material and which is converted by the first enzyme moiety of the first bispecific reagent into the first extra-cellular precipitate, the first extra-cellular precipitate having [at least one of a first] an epitope selected from the group consisting of an antigenic epitope being an epitope which is an integral part of the structure of the first extra-cellular precipitate, a second antigenic epitope, and a neo-antigenic third epitope, the first extra-cellular precipitate forming in the extra-cellular fluid adjacent to the first bispecific reagent and being capable of remaining in the extra-cellular fluid adjacent to the first bispecific reagent for an extended period of time;

continuing the introducing of the first therapeutic agent into the living host to increase the amount of the first extra-cellular precipitate forming in the extra-cellular fluid, the continued administration of the first therapeutic agent thereby causing an accumulation of first extra-cellular precipitate to form in the extra-cellular fluid, the accumulation of the first extra-cellular precipitate thereby having a plurality of antigenic epitopes which is proportional to the amount of accumulation;

Al additionally introducing to the living host a second bispecific reagent having two moieties, a first moiety being a non-mammalian enzyme moiety which is a second enzyme moiety [including], and a second moiety being a targeting agent moiety having a substantial affinity for [at least one of the] an epitope selected from the group consisting of a first antigenic epitope, [the] a second antigenic epitope, and [the] a neo-antigenic third epitope of the first extra-cellular precipitate;

further permitting the second bispecific reagent to bind to [at least one of the] an epitope selected from the group consisting of a first antigenic epitope, [the] a second antigenic epitope, and the neo antigenic third epitope of the first extra-cellular precipitate, the second bispecific reagent being received and bound at the first extra-cellular precipitate which is retained in the extra-cellular fluid for an extended period of time, thereby enabling the second enzyme moiety to convert a substantial amount of an additional therapeutic agent into a new form capable of remaining in the extra-cellular fluid adjacent to the first extra-cellular precipitate for an extended period of time which is sufficient to kill non-selectively all cells

adjacent to the first extra-cellular precipitate; and

a1 additionally administering to the living host the additional therapeutic agent which is a soluble radioactive toxic agent to be converted by the second enzyme moiety into the new form capable of remaining in the extra-cellular fluid adjacent to the first extra-cellular precipitate for an extended period of time which is sufficient to kill non-selectively all cells adjacent to the first extra-cellular precipitate.

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a2 5. (amended) A method in accordance with claim 1 in which the first therapeutic agent is a soluble agent and is an organic chemical [comprising at least one of] selected from the group consisting of peptides, including opio-melanins, of carbohydrates including cellulose, chitosan, and chitin, of proteoglycans, of synthetic polymers, and of indoxyl compounds having molecular positions 1-7.

6. (amended) A method in accordance with claim 1 in which the first therapeutic agent is [inherently] cell impermeant.

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a3 8. (amended) A method in accordance with claim 7 in which the cell-impermeant chemical is selected from the group consisting of [includes one of] thiol, anionic materials, and materials having a molecular weight greater than 1000 daltons.

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a4 13. (amended) A method in accordance with claim 5 in which the indoxyl compounds [include at least one] are selected from the group consisting of indoxyl-penicillin, indoxyl-cephalosporin, indoxyl-glycosides, indoxy-lactam, and the like which when attached to position 3 of the indoxyl compounds are cleavable by the first enzyme moiety of the bispecific reagent, the material remaining after cleaving at position 3 being a soluble reactive intermediate molecule which oxidizes and dimerizes to make a new insoluble molecule which [is insoluble and] forms the first extra-cellular precipitate.

a5 23. (amended) A method in accordance with claim 1 in which the targeting agent moiety of the second bispecific reagent has a substantial affinity for the [first] antigenic epitope of the first extra-cellular precipitate.

a6 26. (amended) A method in accordance with claim 1 in which the additional therapeutic agent is a soluble radioactive toxic agent and is an organic chemical [comprising at least one] selected from the group consisting of peptides, including opio-melanins, of carbohydrates including cellulose, chitosan, and chitin, of proteoglycans, of synthetic polymers, and of indoxyl compounds having molecular positions 1-7.

27. (amended) A method in accordance with claim 1 in which the additional therapeutic agent (inherently) cell impermeant.

29. (amended) A method in accordance with claim 28 in which the cell-impermeant chemical [includes one] is selected from the group consisting of thiol, anionic materials, and materials having a molecular weight greater than 1000 daltons.

34. (amended) A method in accordance with claim 26 in which the indoxyl compounds [include at least one] are selected from the group consisting of indoxyl-penicillin, indoxyl-cephalosporin, indoxyl-glycosides, indoxyl-lactam, and the like which when attached to position 3 of the indoxyl compounds are cleavable by the second enzyme moiety of the second bispecific reagent, the material remaining after cleaving at position 3 being a soluble reactive intermediate molecule which oxidizes and dimerizes to make a new insoluble molecule which is insoluble and forms the second extra-cellular precipitate.

40. (amended) A method in accordance with claim 1 in which the additional therapeutic agent [being the third therapeutic agent] is converted by the second enzyme moiety of the second bispecific reagent into a new form, the new form being a soluble material having a neo-antigenic epitope not present on the [third] additional therapeutic agent from which the new form was created.

41. (amended) A method in accordance with claim 40 in which the [third] additional therapeutic agent is chondroitin sulphate which is converted by the second enzyme moiety of the second bispecific reagent into a new form, the new form of the third therapeutic agent being a soluble material with a neo-antigenic epitope not present on the chondroitin sulphate from which the new form of the [third] additional therapeutic agent was created.

a a 42. (amended) The method in accordance with claim 40 and further comprising the step of administering to the living host a precipitating antibody having a specific affinity for the neo-antigenic epitope on the new form of the [third] additional therapeutic agent, the precipitating antibody being administered prior to the step of administering the [third] additional therapeutic agent, the propitiating antibody [and] having the ability to bind to the neo-antigenic epitope of the new form of the [third] additional therapeutic agent, the binding causing the new form of the [third] additional therapeutic agent to form a third extra-cellular precipitate which remains for an extended period of time adjacent to the relocated first extra-cellular precipitate.

43. (amended) A method according to claim 1 and further comprising the step of administering to the living host a third bispecific reagent to tether the first extra-cellular precipitate, the third bispecific reagent having two moieties, the first moiety having an affinity for [one] an epitope selected from the group consisting of



ag the first antigenic epitope, the second antigenic epitope, and the neo-antigenic third epitope of the first extra-cellular precipitate, the second moiety having an affinity for the third antigenic receptor on the second target cancer cells, the third bispecific reagent being administered prior the administration of the first therapeutic agent and enabling the first extra-cellular precipitate to be retained for an extended period of time adjacent to the third antigenic receptor on the second target cancer cells.

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ag 47. (amended) A method according to claim 1 and further comprising the step of administering to the living host a fourth bispecific reagent, the fourth bispecific reagent having two moieties, the first moiety having an affinity for [one] an epitope selected from the group consisting of the first antigenic epitope, the second antigenic epitope, and the neo-antigenic third epitope of the first extra-cellular precipitate, the second moiety having an affinity for the cancer-altered antigenic epitopes on the cancer-altered extra-cellular matrix, the fourth bispecific reagent being administered prior to the administration of the first therapeutic agent and enabling the first extra-cellular precipitate to be retained for an extended period of time adjacent to the cancer-altered antigenic epitopes on the cancer-altered extra-cellular matrix.

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51. (amended) A method according to claim 1 and further comprising the step of administering to the living host a fifth bispecific reagent, the fifth bispecific reagent having two moieties, the first moiety having an affinity for [one of the] an epitope selected from the group consisting of the first antigenic epitope, the second antigenic epitope, and the neo-antigenic third epitope of the first extra-cellular precipitate, the second moiety having an affinity for the antigenic epitopes on the relocated natural intra-cellular material, the fifth bispecific reagent being administered prior to the administration of the first therapeutic agent and enabling the first extra-cellular precipitate to be retained for an extended period of time adjacent to the antigenic epitopes on the relocated natural intra-cellular material.

55. (amended) A method according to claim 31 and further comprising the step of administering to the living host a sixth bispecific reagent comprised of a molecule having a substantial affinity for [the neo-antigenic epitope of] to the second extra-cellular precipitate, the sixth bispecific reagent being administered prior to the step of additionally administering the second therapeutic agent and enabling the second extra-cellular precipitate to be retained for an extended period of time adjacent to the third antigenic receptor on the second target cancer cells.

69. (amended) A first therapeutic agent being a soluble precipitable material which is adapted to be [disposed adjacent to a] converted into an insoluble and non-digestible precipitate by the action of a non-mammalian enzyme, the first

therapeutic agent when administered to a living host having a heterogeneous population of cancer cells, the heterogenous population of cancer cells including at least a first sub-population of cancer cells being the first target cancer [cell] cells, having a first antigenic receptor, the first therapeutic agent being adapted to be disposed adjacent to the first target cancer cells subsequent to the administration to the living host of a first bispecific reagent, [a] the first bispecific reagent having [a first enzyme moiety being] two moieties, a first moiety which is a non-mammalian enzyme moiety being [bound to] a first enzyme moiety, the first bispecific reagent further having a second moiety including a targeting agent moiety which has a substantial affinity for the first antigenic receptor of the first target cancer [cell] cells, the first therapeutic agent being adapted to be converted in the extra-cellular fluid of the living host, adjacent to the first bispecific reagent, into an insoluble and non-digestible precipitate which is a first extra-cellular precipitate by the action of the first enzyme moiety of the first bispecific reagent, the first bispecific reagent being bound to the first target cancer [cell] cells, the first therapeutic agent [comprising at least one organic chemical of at least one] selected from the group consisting of peptides, including opio-melanins, of carbohydrates including cellulose, chitosan, and chitin, of proteoglycans, of synthetic polymers, and of indoxyl compounds having molecular positions 1-7, the first extra-cellular precipitate having [at least one of] an epitope selected from the group consisting of a first antigenic epitope [being an epitope which is an integral of part of the structure of the first extra-cellular precipitate, a second antigenic

epitope, and a neo-antigenic third epitope, the neo-antigenic third epitope not being present on the first therapeutic agent, the first extra-cellular precipitate remaining in the extra-cellular fluid adjacent to the first bispecific reagent for an extended period of time.

70. (amended) A first therapeutic agent in accordance with claim 69 in which the first therapeutic agent is [inherently] cell impermeant.

72. (amended) A first therapeutic agent in accordance with claim 71 in which the cell-impermeant chemical [includes one] is selected from the group consisting of thiol, anionic materials, and materials having a molecular weight greater than 1000 daltons.

75. (amended) A first therapeutic agent in accordance with claim 74 in which the soluble intermediate molecule is adapted to be [rapidly] naturally oxidized, the oxidized soluble intermediate molecule being adapted to be spontaneously dimerized [and], thereby forming the first extra-cellular precipitate.

76. (amended) A first therapeutic agent in accordance with claim 69 in which each of the indoxyl compounds [include at least one] are selected from the group consisting of indoxyl-lactam[indoxyl-penicillin, indoxyl-cephalosporin,] indoxyl-glycosides, and the like which when attached to position 3 of the indoxyl